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Periodontal chemotherapeutics: systemic and local antibiotics

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Introduction

The primary etiology of periodontitis is bacterial plaque in a susceptible host.[1,2] Periodontal therapy is tailored according to individual patient's needs and there is not a universal treatment plan for all periodontitis patients.

Periodontal pathogens are complex and heterogenous, with at least 500 species culturable from periodontal pockets.[3] The most commonly identified are anaerobic Gram negative rods such as *P. gingivalis, P. intermedia, F. nucleatum.* The remaining consist of Gram-postive facultative and anerobic cocci and rods and Gram-negative facultative rods.[3] *A.actinomycetemcomitans*, a well known periodontal pathogen, possesses numerous virulence factors including the ability to penetrate into soft tissue and evade the host defense mechanisms.[4] Mechanical debridement alone will not be sufficient; surgical and/or chemotherapeutic approaches should be considered.[5, 6]

Goals for periodontal therapy include: 1) removal of pathogenic bacterial plaque and calculus, 2) disruption of the subgingival plaque biofilm, 3) surgical procedures to reduce probing depths and/or regenerate lost periodontium, 4) maintaining a healthy periodontium. Studies show that elimination or suppression of periodontal pathogens will decrease probing depths and bleeding upon probing.[7] Due to limited visibility and access to subgingival areas and the tenacious character of calculus,[8] reduction of pathogenic bacteria to the level compatable with health can be difficult to achieve.

Chemotherapeutics were introduced to assist in reducing microflora and optimizing the host response. The purpose of this update is to describe the rationale and recommended protocol for use of systemic, localized delivery antibiotics and subantimicrobial dose doxycycline in periodontics.

Systemic antibiotics

Medical/dental history review should be thoroughly investigated and the establishment of proper diagnoses identified prior to treatment. Periodontal treatment plan should include oral hygiene instructions, scaling and root planing (SRP) and a re-evaluation of the periodontium 4-6 weeks later. Most patients will respond with improved clinical parameters: probing depth reduction and clinical attachment gain. For patients who do not respond well to conventional therapy, antibiotics can be used as an adjunct mode of therapy. Culture and sensitivity (C & S) testing is highly recommended prior to the administration of systemic antibiotics because an inappropriate prescription can lead to increased microbial resistance and poor host response.

If C & S testing is not possible, the following regimen of systemic antibiotics can be considered for patients with the following diagnoses, based on several studies:

1) Aggressive periodontitis:
   a) Localized: amoxicillin and metronidazole 250mg each tid x 7d.[9]
   b) Generalized: amox/metro 500mg each tid x 7d.[10]
2) Refractory periodontitis: clindamycin 150mg qid x 7d.[11]
3) Periodontal abcess with systemic symptoms: amox 500mg tid x 7d or penicillin 500mg qid x 7 d.
4) Necrotizing ulcerative gingivitis/periodontitis (NUG/NUP): metro 250mg tid x 7d.[12]

Despite reported improved clinical results, systemic antibiotics are not without disadvantages. Bacterial resistance, patient compliance and the inability to achieve high concentrations in the sulcus are a few disadvantages to be considered in your treatment rationale.

Local delivery antimicrobial agents (LDAs)

The advantage of LDAs is the higher concentration or lethal dose of medicament achieved in the periodontal pocket compared to systemic antibiotics. In order for the agent to be effective, it must deliver a concentration greater than the minimum inhibitory concentration (MIC^{90}) for periodontal pathogens and have substantivity.[13] The level achievable for chlorhexidine (CHX) is 1300-1900 mcg/ml (MIC^{90} 100mcg/ml),[14, 17] 10% doxycycline gel is 250mcg/ml (MIC^{90} 6mcg/ml)[15, 17] and 1 mg minocycline microspheres is 340 mcg/ml (MIC^{90} 16mcg/ml).[16, 17] In addition, there has been no evidence of major adverse patient complications with the use of LDAs.[18]

There are three FDA-approved products currently available in the US: 1) Atridox® (10% doxycycline in biodegradable polymer) is applied with a syringe into the periodontal pocket and for 21 days the antibiotic is slowly released to the surrounding site. Abstinence from brushing or flossing in treated sites for 7 days is recommended. 2) PerioChip® (2.5 mg chlorhexidine in gelatin carrier) is self-retentive and degrades in 14 days. Flossing and brushing in the treated sites is not recommended until the product self degrades. 3) Arestin® (1 mg minocycline HCL in polyglycolide microspheres) is a powder that becomes bioadhesive upon gingival crevicular fluid (GCF) contact. It has an extended release for up to 21 days. Brushing for 24 hours and interproximal cleaning for 10 days are prohibited post-placement. Detailed instructions can be found for each product on the manufacturers' websites. According to the American Academy of Periodontology, the use of LDAs in chronic periodontitis patients in conjunction with SRP is recommended "when localized recurrent and/or residual probing depth (PD) of greater than or equal to 5mm with inflammation still present following conventional therapies." Bleeding on probing is an indicator of inflammation. LDAs are not indicated when intrabony defects are present, multiple sites in the same quadrant with greater than or equal to 5mm PD or if LDAs have failed previously to reduce PD or control periodontitis. LDAs are not meant to replace proper periodontal therapy. [19]

LDAs should be used with discretion since there is no evidence to support the use of LDAs to reduce the need for surgery, to control

costs or to prevent tooth loss.[19] There is insufficient evidence to use LDAs in special situations such as with peri-implantitis, periodontal abcesses, smokers, aggressive periodontitis or medically compromised patients.[19]

Subantimicrobial dose doxycycline (SDD)

There is a large body of evidence suggesting the host's inflammatory response to the bacterial challenge contributes to the progression of periodontal disease. Polymorphonuclear leukocytes (PMNs) respond to the intial accumulation of bacterial plaque in the sulcus. Eventually the chronic exposure to bacterial plaque will initiate the recruitment of other immune cells/leukocytes. Numerous inflammatory mediators such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNFα), C-reactive protein (CRP) and matrix metalloproteinases (MMP) are released to defend the host and propagate the inflammatory response.[2] Unfortuantely, unless the plaque is reduced to a level tolerated by the host, a chronic inflammatory state exists. Like other chronic inflammatory conditions, the inevitable destruction of host tissue results. Host modulation therapy (HMT) addresses the immune-inflammation defense mechanism in response to the presence of bacterial plaque. SDD (Periostat®) is a long-term therapy of low-dose doxycyline. Mechanism of action includes the decreased production of the destructive host's MMPs, which are collagenases released by PMNs. Combined with traditional periodontal therapy, controlling the inflammation induced by bacteria has shown to be benefical. [20] Periostat is prescribed as 20mg b.i.d. for 3 months with re-evaluation to determine the need for further treatment.

Summary

Antibiotics can be beneficial in the treatment of periodontitis. However, due to the complex etiology of periodontitis, careful evaluation should be rendered prior to the administration of antibiotics. The following is a guideline to periodontal antibiotic therapy. 1) Initial therapy to include oral hygiene instructions and mechanical root debridement. 2) Re-evaluation in 4-6 weeks. 3) Antibiotics may be prescribed based on medical status, C & S test results, and clinical needs of the patient. 4) Re-evaluation and surgical plan can be formulated according to patient's response. 5) Clinical response should be re-evaluated again in 1-3 months. 6) If resolution of the periodontal infection is achieved, an individual maintenance program is established for the patient.

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